Glycosyl Trichloroacetimidate | Thioglycoside | Glycosyl Sulfoxide | Glycosyl Halide | Glycosyl Phosphite | Pentenyl Glycoside | 1,2-Anhydrosugar

Figure 1 Commonly used glycosylating agents

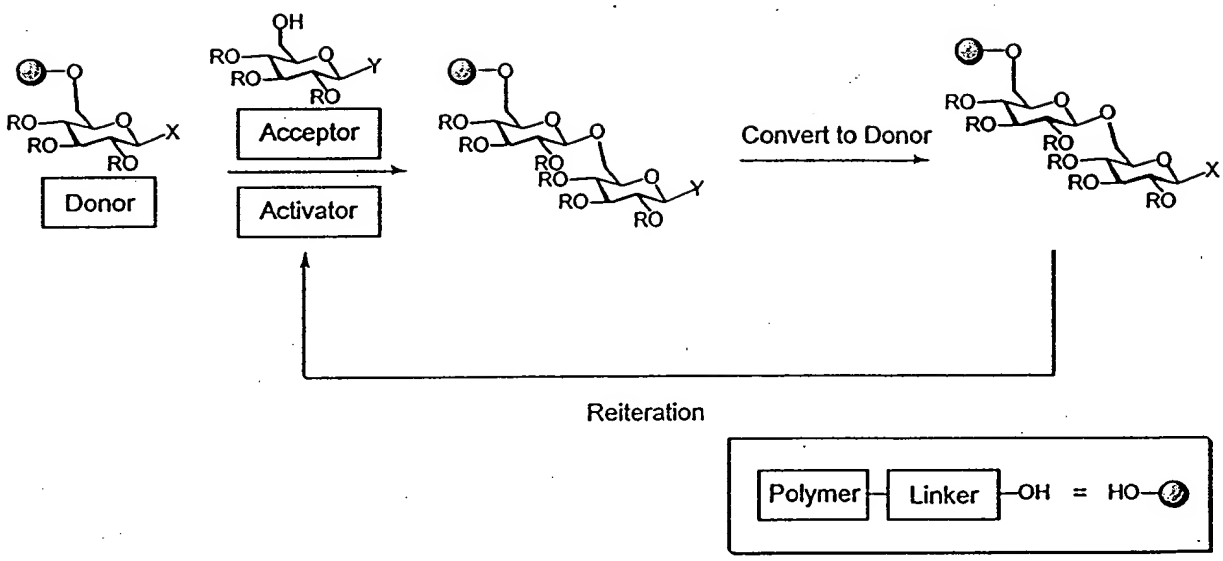


Figure 2 Donor bound solid-phase carbohydrate synthesis

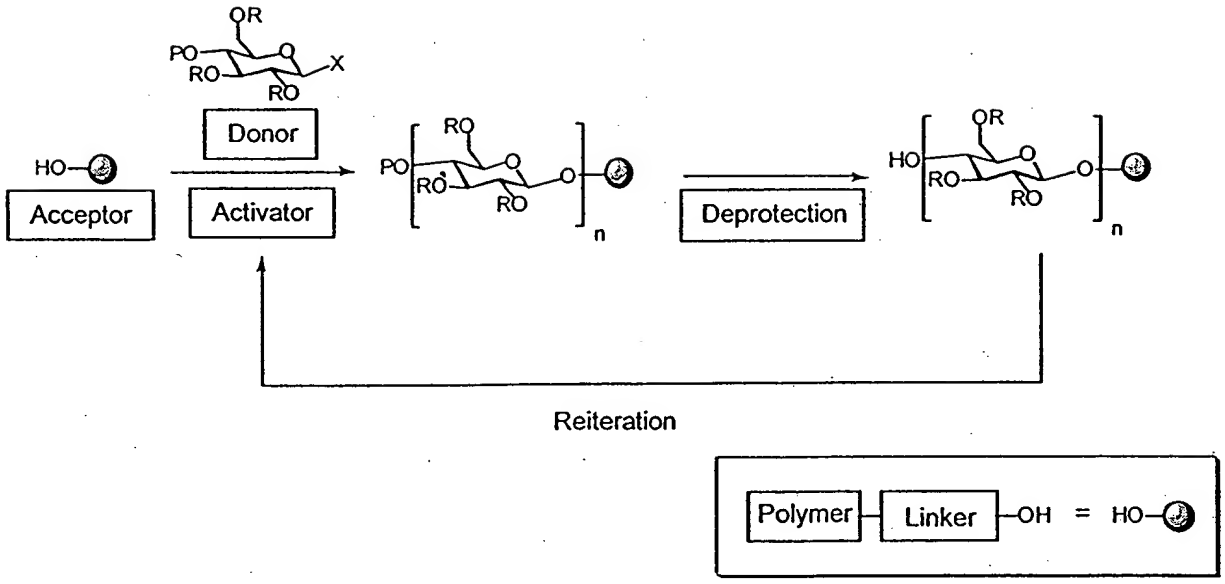
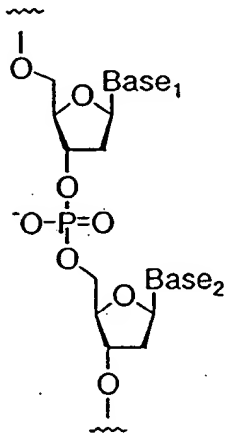


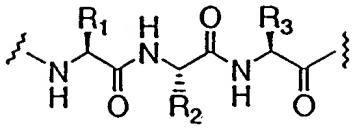
Figure 3 Acceptor bound solid-phase carbohydrate synthesis

Figure 4

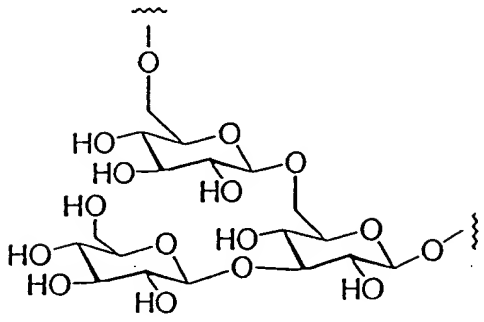
a) oligonucleotides



b) oligopeptides



c) oligosaccharides



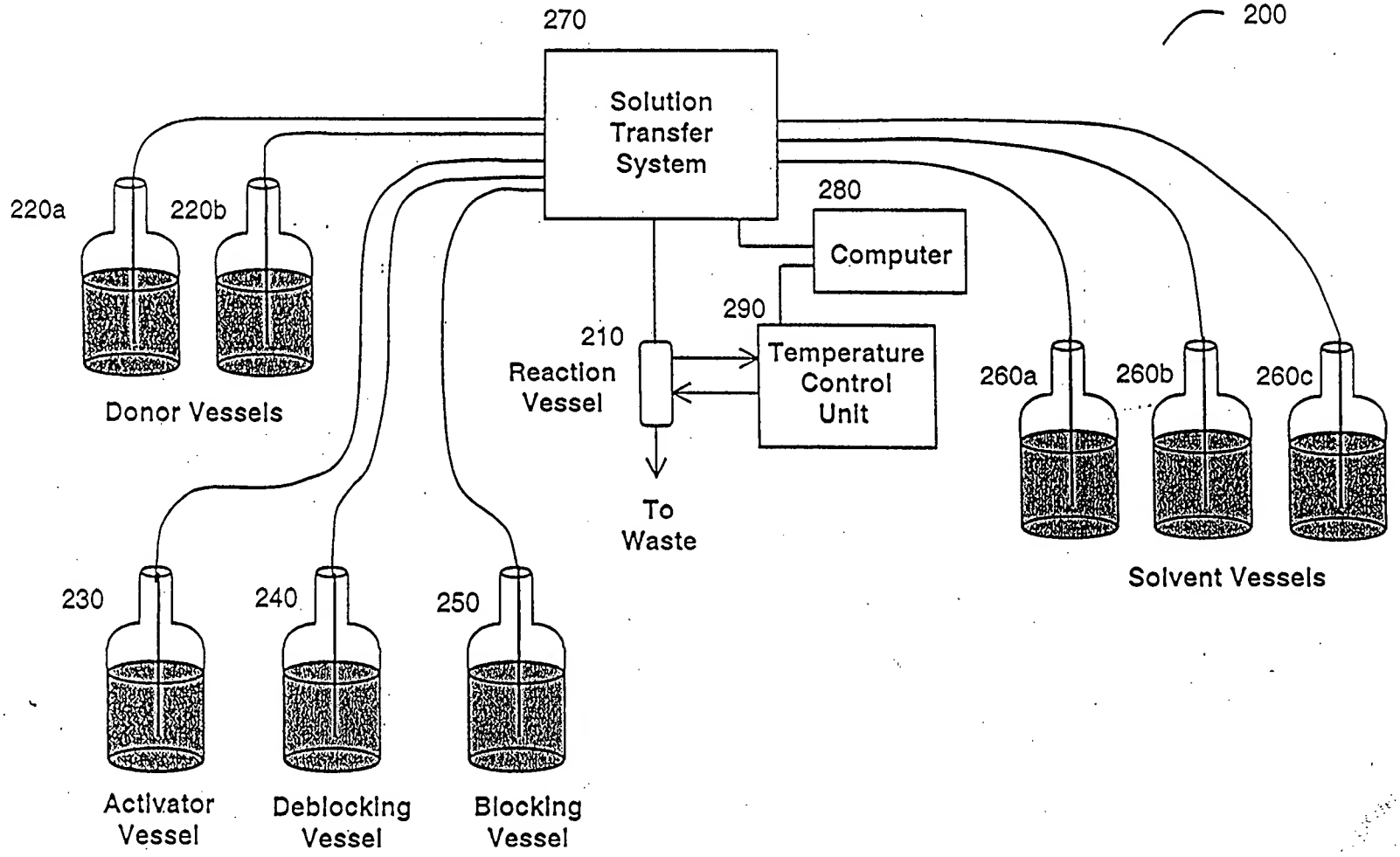

Automated Oligosaccharide Synthesizer
270
200
Solution
Transfer
System
220a
220b
Donor Vessels
280
Computer
290
210
Reaction
Vessel
Temperature
Control
Unit
To
Waste
260a
260b
260c
Solvent Vessels
230
240
250
Activator
Vessel
Deblocking
Vessel
Blocking
Vessel

Figure 5

Automated Oligosaccharide Synthesizer

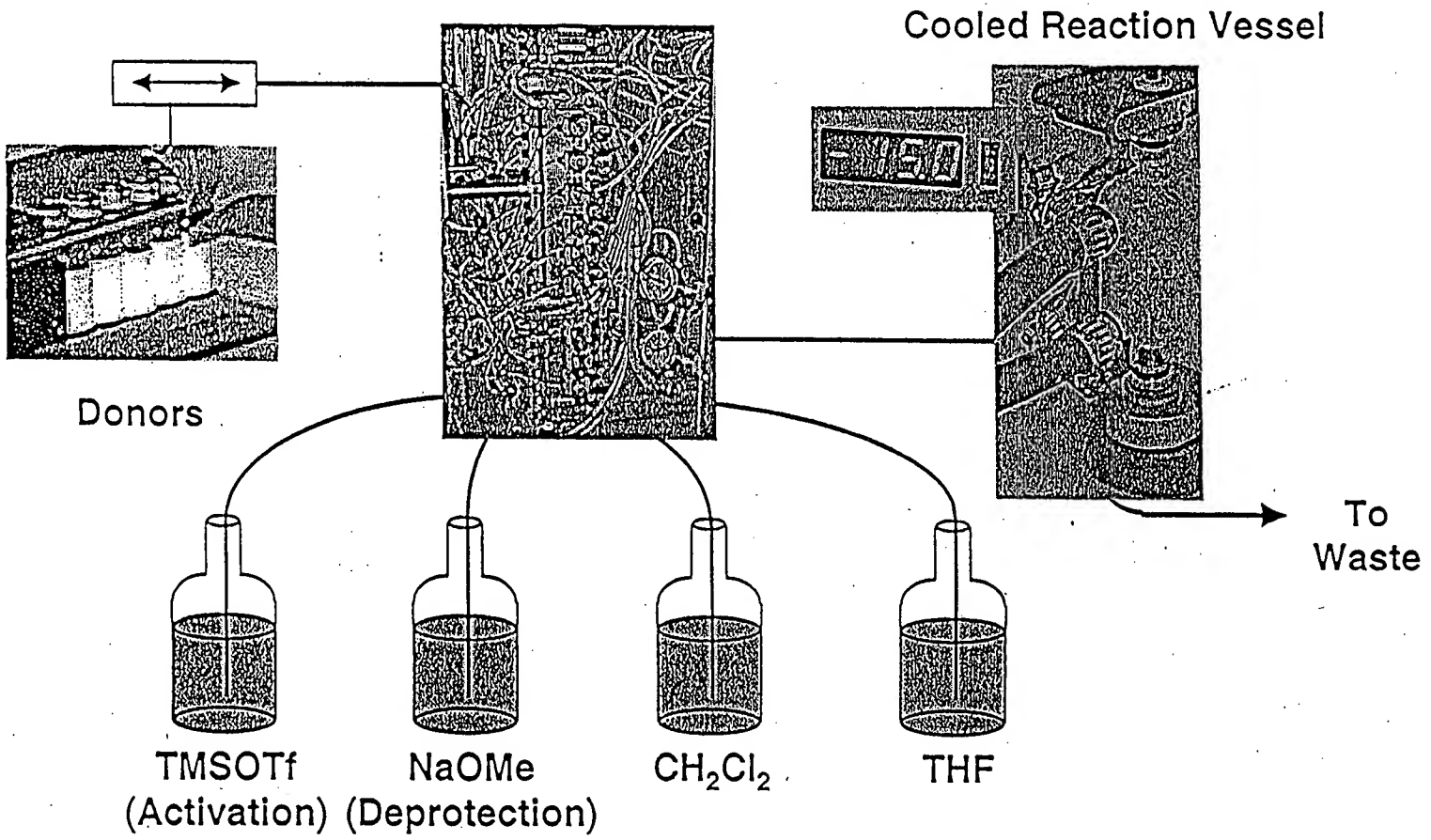


Figure 6

Double-Walled Cooled Reaction Vessel

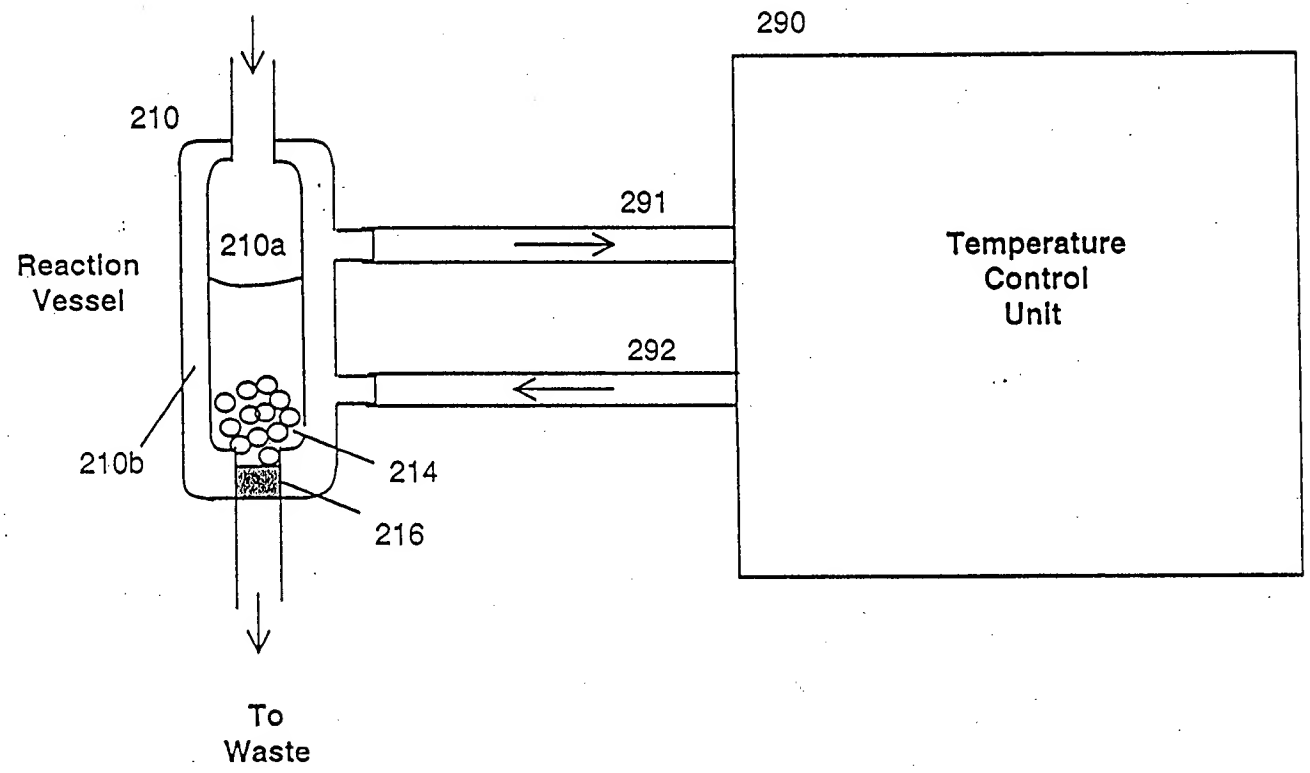
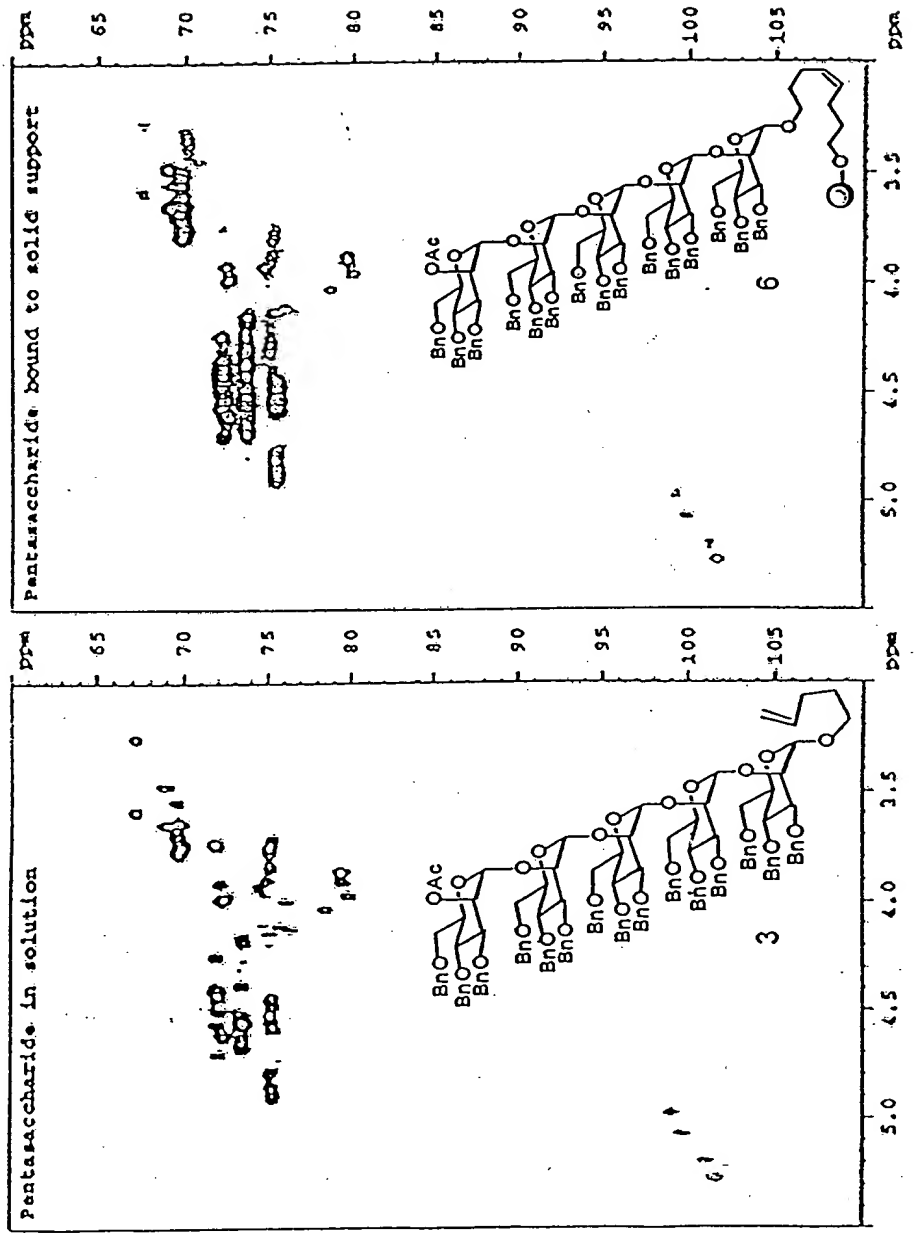


Figure 7

Figure 8

2D-NMR comparison of resin bound and solution phase pentamer



Automated Synthesis of the Phytoalexin Elicitor β-Glucan Using Glycosyl Phosphates

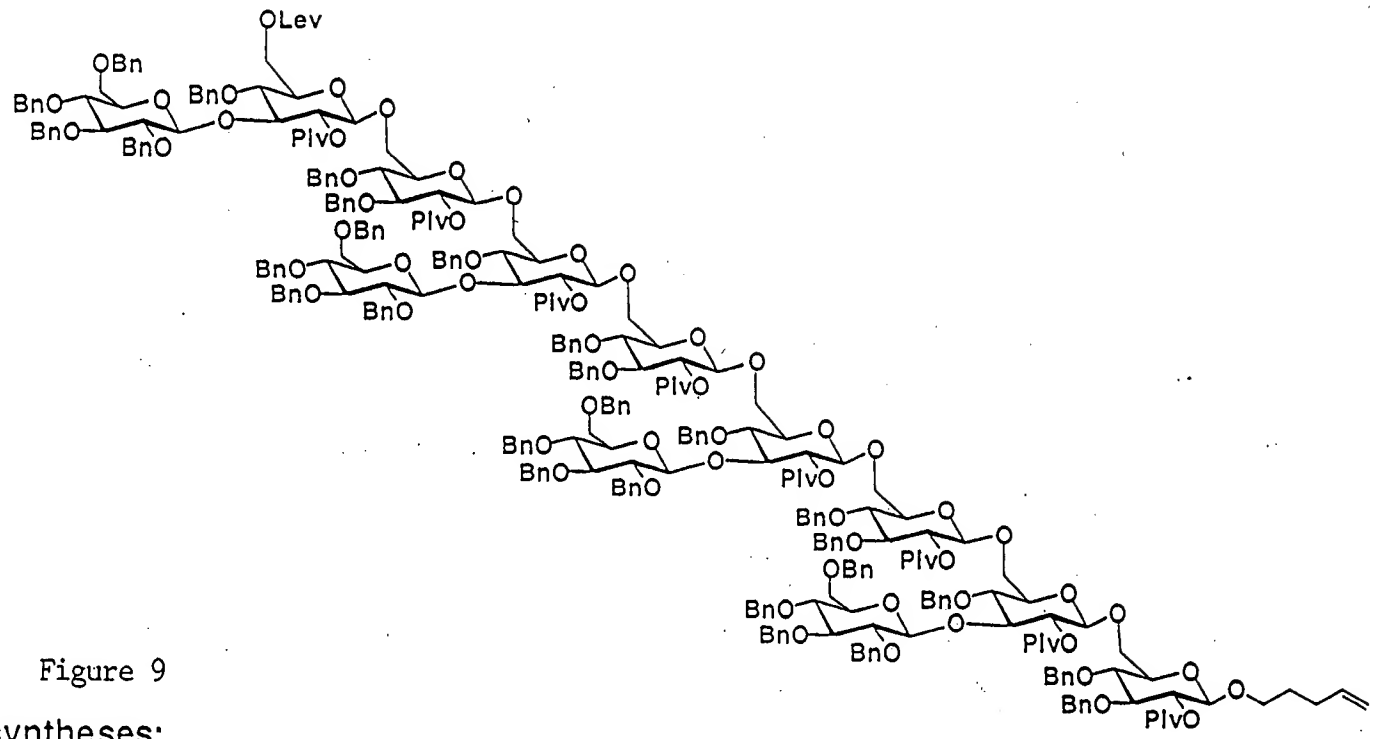


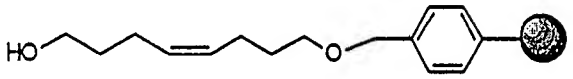
Figure 9

Prior syntheses:
Garegg et al. *Angew. Chem. Int. Ed.* 1983, *22*, 793;
van Boom et al. *Chem. Eur. J.* 1995, *1*, 16;
on soluble support: van Boom et al. *Recl. Trav. Chim. Pays-Bas* 1993, *112*, 464;
on polymer support using trisaccharide blocks: Nicolaou et al. *Angew. Chem. Int. Ed.* 1998, *37*, 1559.

Figure 10

Automated Oligosaccharide Synthesis

Chemical Issues:

- Choice of Resin (Merrifield's, Argopore, Tentagel)
- Linker: 

- Glycosylation Protocol
- Deprotection Protocol
- Capping Cycle
- Cleavage Method
- Purification Technique

Practical Issues:

- Scale (μmol-mmol)
- Cycle Development/Time
- Temperature Control Device

Automated Oligosaccharide Synthesis with Glycosyl Phosphates: Coupling Cycle

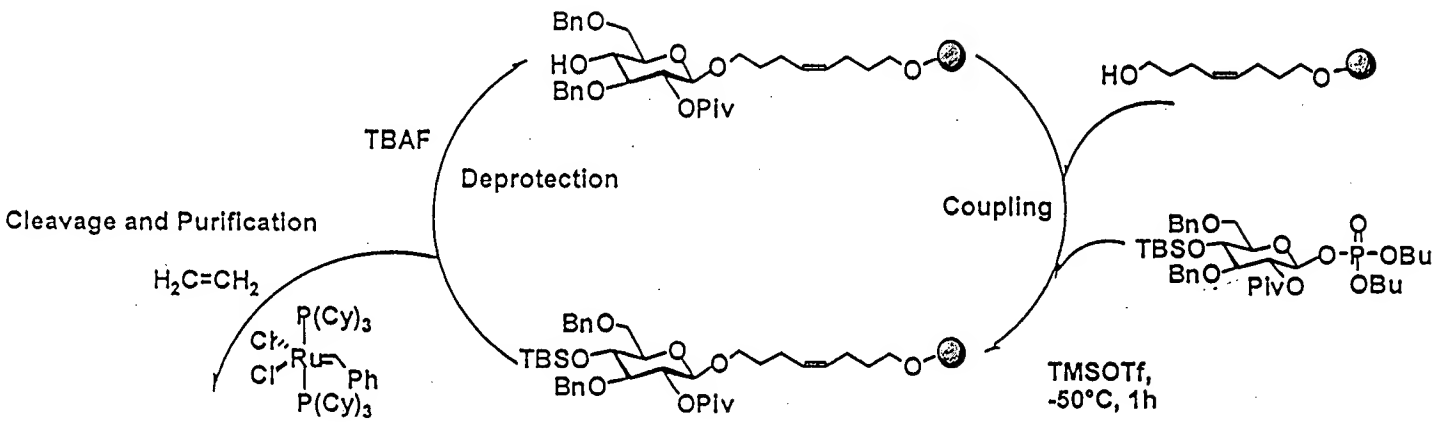
	Reagent/Solvent	Equivalents	Temperature	Time
Coupling	Donor	5	-15 °C	15 min
	TMSOTf	5		
Washing	CH_2Cl_2			
	THF			5 min
Coupling	Donor	5	-15 °C	15 min
	TMSOTf	5		
Washing	CH_2Cl_2			
	THF			5 min
Deprotection	N_2H_4-HOAc		15 °C	30 min
Washing	Pyr./AcOH			5 min
Deprotection	N_2H_4-HOAc		15 °C	30 min
Washing	Pyr./AcOH			5 min
			Cycle Time per residue	110 min

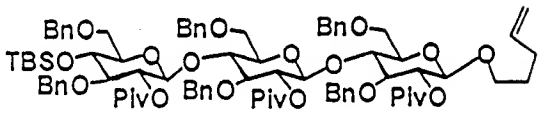
Figure 11

11/22

Figure 12

Solid Support Oligosaccharide Synthesis: Glycosyl Phosphate Donors



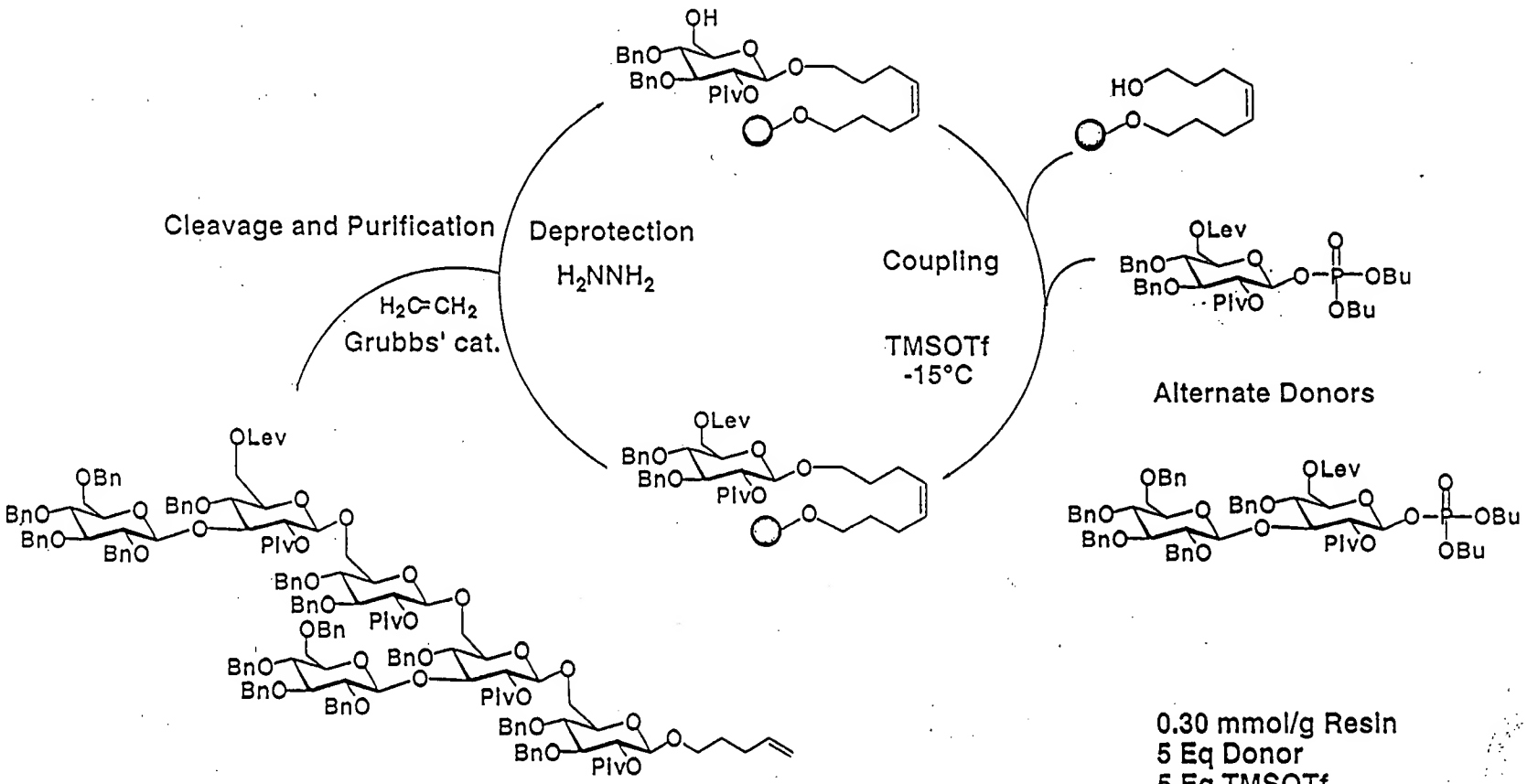


53% overall yield

Advantages:
- excess reagents drive reactions to completion
- purification only at the end of the synthesis

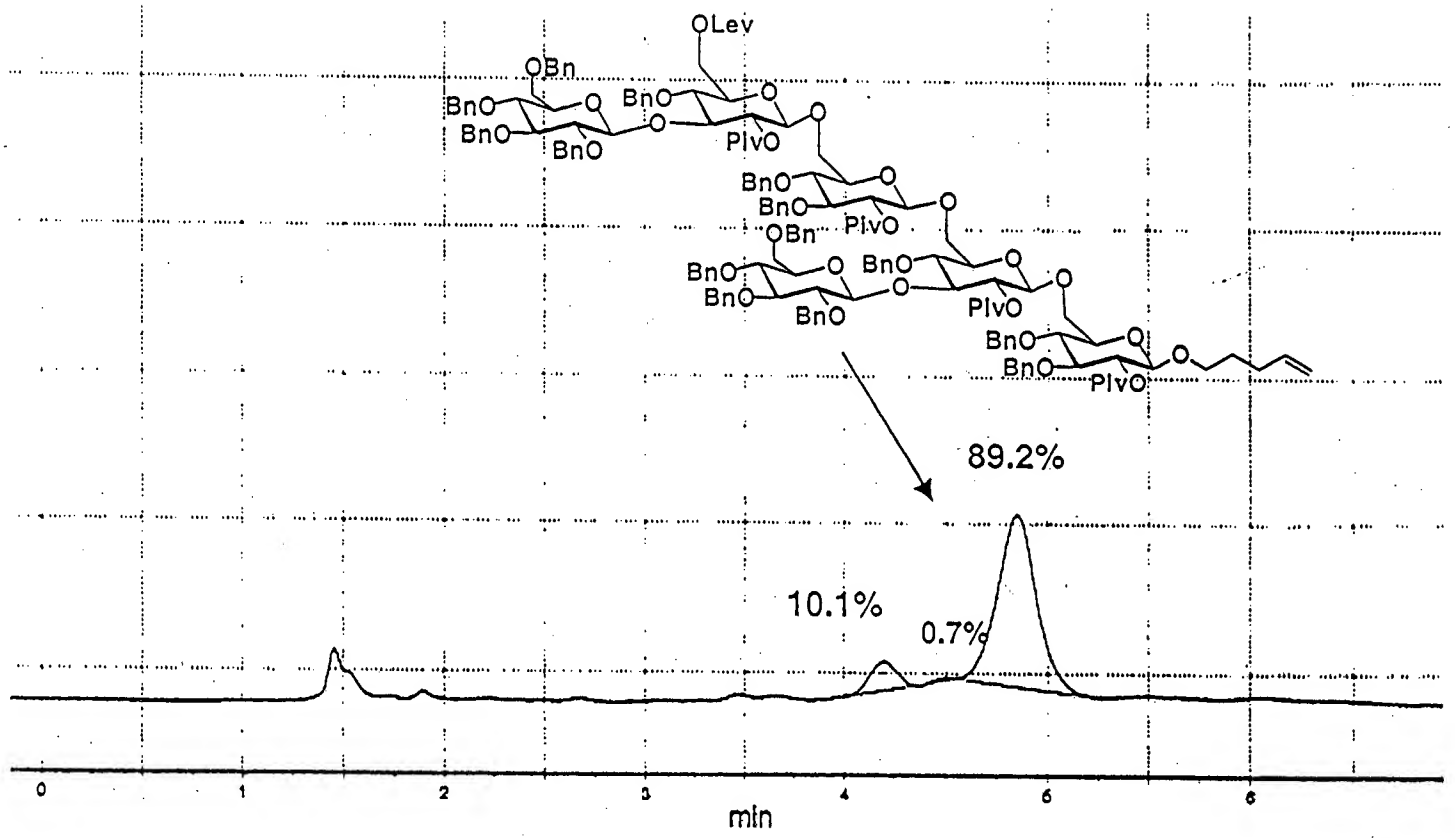
Figure 13

Automated Hexasaccharide Synthesis Using Glycosyl Phosphates



Crude HPLC Profile of the Hexamer Synthesis

Figure 14



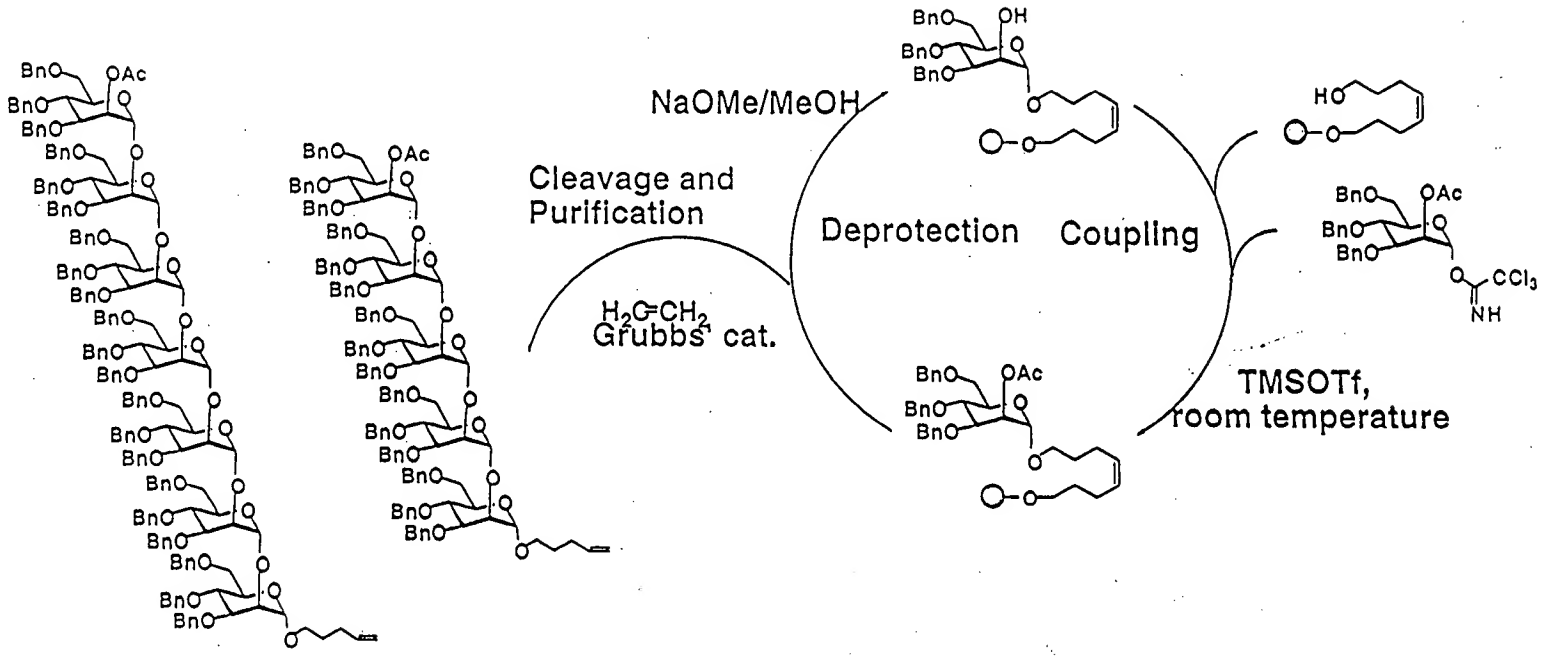
Automated Oligomannoside Synthesis: Coupling Cycle

	Reagent/Solvent	Equivalents	Time
Coupling	Donor	10	30 min
	TMSOTf	0.5	
Washing	CH_2Cl_2		5 min
	THF		
Coupling	Donor	10	30 min
	TMSOTf	0.5	
Washing	CH_2Cl_2		5 min
	THF		
Deprotection	NaOMe		30 min
Washing	CH_2Cl_2		5 min
	THF		
Deprotection	NaOMe		30 min
Washing	CH_2Cl_2		5 min
	THF		
25μmol Scale	Cycle Time per residue		140 min

Figure 15

Solid-Phase Oligosaccharide Synthesis: Coupling Cycle Development

Figure 16



42% yield 74% yield

(manual synthesis: 9%)

stepwise yield: 94% stepwise yield: 94%

Figure 17

HR-MAS HMQC-Analysis of Pentamannosides